

# Diagnostic Problems in Luetic Cardiovascular Disease \*

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**I. GENERAL CONSIDERATIONS:** The prevention of cardiovascular syphilis is the prevention of syphilis itself. In 1929 Bruusgaard<sup>3</sup> reported that of 473 patients who had received no anti-luetic treatment, 10 per cent had developed clinical evidences of cardiovascular lues. The average duration of syphilis in this group was 20 years. These data are in agreement with those of Turner,<sup>17</sup> who made a similar analysis of approximately 6,000 cases of late untreated syphilis at the Johns Hopkins Clinic. In 1937, Kemp and Cochems<sup>4</sup> reported an incidence of 12.7 per cent of cardiovascular involvement in a series of 1,000 luetics. There is abundant evidence in the literature to show that clinical involvement of the cardiovascular system will develop in approximately 10 per cent of untreated or inadequately treated cases of acquired syphilis. Post-mortem examinations reveal that in all instances where a pathological diagnosis of late syphilis can be established, 70-90 per cent of the subjects show evidences of cardiovascular lues.<sup>5,18</sup> Although these figures are based primarily upon microscopic changes, they serve to emphasize to the clinician the importance of being on the alert for signs or symptoms referable to the cardiovascular system in the patient afflicted with lues. From the very beginning syphilis is a vascular disease. Much has been written on the pathology of syphilis, particularly with respect to its protean manifestations, its predilection for the supralvalvular portion of the ascending aorta, and its tendency to produce low-grade inflammatory changes in the media and adventitia of the ascending, transverse, and less frequently, the descending limb of the aorta.<sup>8</sup> The earliest involvement of the aorta is due to low-grade inflammatory processes in the adventitia and media of the ascending aorta not attended by gross anatomical alterations or symptoms. Secondly, there may be sufficient involvement of the elastica to account for dilatation of the aortic wall. Thirdly, there may be local destruction of the elastica followed by the formation of an aneurysm. Fourthly, the supralvalvular portion of the aorta may undergo lowgrade inflammatory changes, with resultant fibrosis and scarring of the valve leaflets or there may be sufficient retraction of the valve leaflets to produce frank aortic insufficiency. Lastly, there may be narrowing of the coronary ostia as a result of the progressive fibrotic changes which have occurred in the walls of the aorta.

After varying lapses of time, these changes or any combination of them may follow the initial infection. In general it is believed that the diagnosis of cardiovascular syphilis becomes recog-

nizable about 10 to 30 years after the primary infection. Furthermore, it must be remembered that approximately 50 per cent of the clinically detectable lesions of late syphilis are referable to the cardiovascular system.

The importance of establishing the diagnosis of luetic cardiovascular disease at the earliest possible time has been emphasized by several investigators,<sup>9,10,12,16</sup> and the effect of instituting early treatment is best summarized by Moore<sup>8</sup>:

The Incidence and Prognosis of Life Span in Patients with Various Types of Cardiovascular Complications in Late Syphilis.

Clinical Type	Percentage of Patients Affected	Prognosis	
		Untreated	Treated
Uncomplicated aortitis clinically unrecognizable ...	70-90	Good	Excellent
Uncomplicated aortitis, recognizable on basis of symptoms and signs....	5-10	5-10 years	10-20 years
Aortitis with saccular aneurysm .....	1-2	1-2 years	5-10 years
Aortitis with aortic regurgitation .....	2-3	2-3 years	4-10 years

Many criteria have been given in order to evaluate the various signs and symptoms of uncomplicated aortitis.<sup>1,2,7,10,11,13,14,15</sup> The relative importance of these varies from observer to observer. In regard to the order of frequency and importance, uncomplicated luetic aortitis may be diagnosed when: (1) There is roentgenographic evidence of aortic dilatation; (2) The aortic second sound is hollow or of tambour quality; (3) There is dyspnea; and (4) There is sub-sternal pain. In addition the patient should be under 40 years of age, free of hypertension, arteriosclerosis and other cardiovascular diseases which might produce identical signs and symptoms.<sup>6</sup> On the other hand the diagnosis of frank aortic insufficiency or of aneurysm seldom proves difficult.

**II. ORGANIZATION AND PURPOSE OF THE LUETIC CARDIOVASCULAR CLINIC.** In 1939, a special cardiovascular clinic for luetic out-patients was organized at the University of California. It was conducted by three full-time members of the medical staff in cooperation with the director of the clinic for luetics. Its purposes were to provide a diagnostic and advisory center, a uniform type of examination, a uniform type of record, and to make data available for teaching and research purposes. It was the intention of the group to give special consideration to the criteria suggested above and to determine to what extent it would be possible to make reliable diagnoses of early cardiovascular lues under the usual conditions found in

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an out-patient department. Ideally all patients who were seen in the clinic for luetics would be referred to the cardiovascular clinic and thus provide unselected material for statistical evaluation of diagnosis and treatment during the ensuing years.

The examination form used in the clinic was designed to obtain a complete cardiovascular history on each patient, with especial reference to the presence of pre-cordial pain, dyspnea, hemoptysis, cough, sputum, hoarseness, vertigo, edema, palpitation, indigestion, insomnia, weakness or other symptoms referable to the cardiovascular system. Space is provided on the form for the following special observations in the physical examination: the point of maximum intensity, the area of cardiac dullness (right border and left border), area of the base, thrills, murmurs, character of heart sounds including the aortic second sound, rate, character and rhythm of the pulse, blood pressure in each arm, and signs of arteriosclerosis. Provision is made for recording notes on the presence of the following: occlusion of peripheral vessels, episternal notch pulsation, diastolic shock, capillary pulsation, visible arterial pulsation and femoral pistol shot sounds. At the bottom of the form are listed the results of the teleoroentgenogram, fluoroscopy and electrocardiogram, followed by the diagnosis and recommendations for treatment.

At the completion of the examination, a working diagnosis was made, and recommendations for treatment were suggested to the staff in charge of the treatment of luetic patients. Adequate clinical follow-up was to be provided by scheduled return appointments for all patients examined in the luetic cardiovascular clinic.

III. ANALYSIS OF DATA. During the five-year period covered by this study, approximately 2,000 patients were seen in the Luetic Clinic, and of these, 355 were given the cardiovascular examination as outlined in the special clinic. Therefore, it was impossible to make an accurate statement concerning the incidence of luetic involvement of the cardiovascular system in patients afflicted with syphilis. Those patients who were examined represented neither a random nor a selected sample of the population at risk.

In figures 1 and 2 are shown the age distribution of the patients seen in the luetic cardiovascular clinic. The majority of patients fell within the age group of 35 to 60 years. Of the total number of women, 71 per cent of the afflicted were over 40 years of age; and among the males, 85 per cent were over 40 years of age. Of the total afflicted subjects, less than one-third were women.

In figure 3 is given the number of sero-positive patients (132 or 34 per cent) in whom the diagnosis of no cardiovascular disease was made. The majority of these fell within the age group of 30 to 55 years. In general, those sero-positive patients having no cardiovascular disease tended to be younger than those sero-positive patients in whom the diagnosis of arteriosclerotic or hypertensive heart disease occurred (figure 4). The

latter group comprised 114 cases or 29 per cent of the total. The major portion of these patients were between the ages of 45 and 65 years.

In figure 5 is demonstrated the incidence of the diagnosis of luetic cardiovascular disease of all types—136 cases or 35 per cent of the total. This graph demonstrates that in the age groups under consideration, luetic cardiovascular disease occurs most frequently in those age groups which also suffer from the highest incidence of arteriosclerotic or hypertensive heart disease. In other words, with rare exceptions, it is uncommon in this series of observations to find patients with luetic cardiovascular disease unaccompanied by

Luetic Cardiovascular Clinic ~ 1939-1944

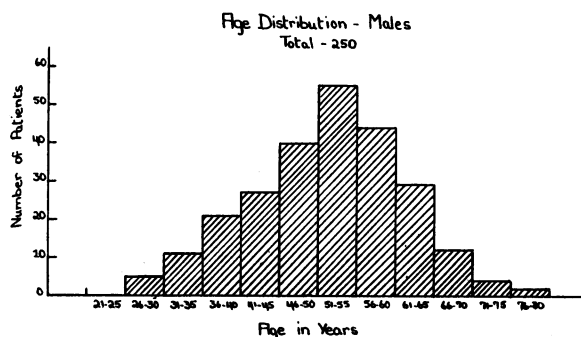


FIGURE 1

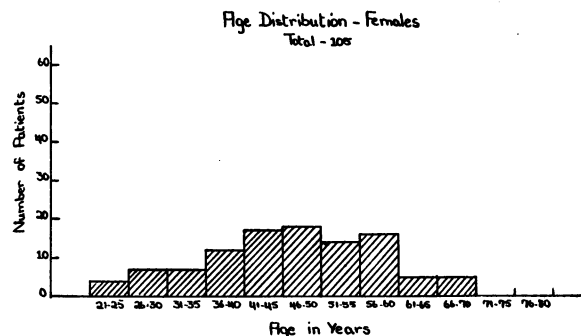


FIGURE 2

Incidence of Sero-Positive Patients  
Diagnosed as Having No Cardiovascular Disease

Total: 132 cases ~ 34% of 355 cases

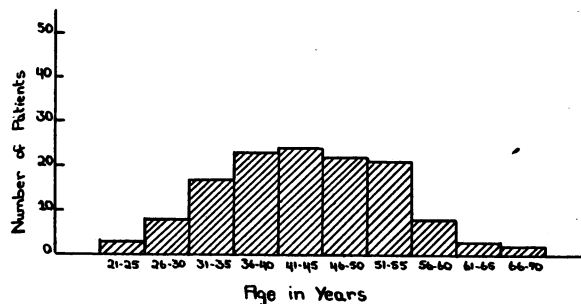


FIGURE 3

Incidence of Diagnosis of  
Arteriosclerotic or Hypertensive Heart Disease  
in Patients Having Serological Lues.

Total: 114 cases ~ 29% of 355 cases

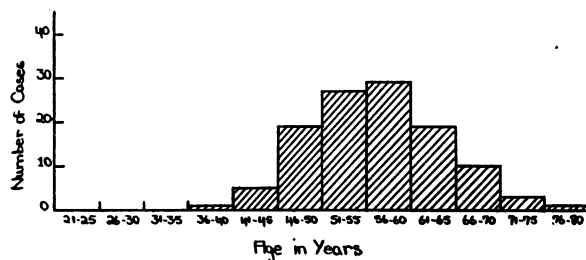


FIGURE 4

Incidence of Diagnosis of  
Luetic Cardiovascular Disease - All Types

Total: 136 cases ~ 35% of 355 cases

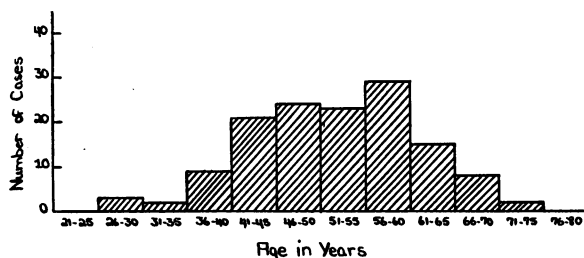


FIGURE 5

arteriosclerotic or hypertensive changes. As has been stated before, these latter changes may produce signs or symptoms which fulfill the criteria designated for luetic aortic involvement.

In Table I is recorded the distribution of diagnoses for the total group of 353 patients (one patient having been omitted because of congenital lues, and one because of a complicating mediastinal tumor). Since in many patients there was more than one diagnosis, the total number of

VARIETY OF CARDIOVASCULAR DIAGNOSES  
IN GROUP UNDER STUDY - 353 PATIENTS

Diagnosis	Number of Cases	% of Total Diagnoses
Luetic Aortitis	33	9
Aortic Insufficiency	40	10
Aortic Aneurysm	63	16
Mixed Valvular Disease	6	2
Hypertension and/or Arteriosclerosis	114	29
No Cardiovascular Disease	132	34
<b>Total Diagnoses</b>	<b>388</b>	

Table I

diagnoses (388) exceeds the total number of patients (353). Of the total diagnoses 34 per cent are listed as having no cardiovascular disease; 29 per cent as having hypertensive or arteriosclerotic heart disease; and 35 per cent as having luetic cardiovascular disease—and of these 9 per cent luetic aortitis, 10 per cent aortic insufficiency, 16 per cent aortic aneurysm, and 2 per cent were listed as having rheumatic heart disease with mixed valvular lesions.

In Table II is shown the age distribution of the three primary luetic cardiovascular diseases: aortitis, aortic insufficiency, and aortic aneurysm. It will be noted that the graver forms of luetic cardiovascular disease occur in the progressively older age groups and that the highest incidences occur after the age of 40 years. These data provide further evidence of the part which arteriosclerosis and hypertension plays in the onset of luetic cardiovascular disease.

In Table III is given the incidence of cardiovascular disease with respect to the time interval elapsing between the primary luetic infection and the date of observation. Of the total 355 subjects, 56 per cent had no knowledge of the date of infection, a figure in agreement with that of most observers. There appears to be very little difference in the interval of lapsed time between the primary infection and the onset of cardiovascular signs or symptoms in the group suffering from luetic cardiovascular disease when contrasted with the group suffering from arteriosclerotic or hypertensive heart disease.

It is possible that the incidence of cardiovascular disease, whether luetic, arteriosclerotic or hypertensive, may be a function of age rather than of duration of the infection. The exception to this statement appears to be in the group diagnosed luetic aortitis, where 18 per cent of the cases had a lapse of 11 to 15 years before the onset of cardiovascular symptoms. According to the criteria set down, aortitis is the most difficult to diagnose and hence the most likely to be over-diagnosed.

In Table IV the presenting complaints of all patients are listed according to diagnoses. As might be expected, those patients diagnosed as having no cardiovascular disease had fewer symptoms than those in the other diagnostic groups. The two most common complaints for all groups were dyspnea and chest pain, and these symptoms occurred more frequently in those patients who suffered from luetic cardiovascular disease.

In Table V the prominent physical findings of 347 patients are recorded according to diagnosis. Here again there have been multiple diagnoses on certain patients, and therefore the total number of diagnoses exceeds the total number of cases. Cardiac enlargement was observed in 39 per cent of patients having a diagnosis of aortitis, in 57 per cent with a diagnosis of aortic insufficiency, in 43 per cent with aortic aneurysm, in 25 per cent with arteriosclerosis or hypertension, and in 2 per cent of patients thought to have no cardiovascular disease. A tambour aortic second sound was encountered rather frequently in subjects suffering

## AGE INCIDENCE OF LUETIC CARDIOVASCULAR DISEASE

TOTAL: 136 CASES - 35% OF 355 CASES

Diagnosis	No. of Cases	Percent of Cases by Age Group										
		21-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75
Luetic Aortitis	33		3	3	12	21	18	15	18	9		
Aortic Insufficiency	40		5	2	8	12	20	20	12	12	8	
Aortic Aneurysm	63				3	14	16	16	29	11	8	3

Table II

## INCIDENCE OF CARDIOVASCULAR DISEASE

WITH RESPECT TO INTERVAL ELAPSING FROM PRIMARY LUETIC INFECTION

Diagnosis	No. of Cases	Percent of Cases by Years Elapsed									
		1-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	41-45	Unkn.
Luetic Cardiovascular Disease (All Types)	136	2	2	7	7	3	11	6	6	5	50
Luetic Aortitis	33	6	-	18	9	3	12	3	3	3	42
Aortic Insufficiency	40	2	2	5	5	5	8	10	5	8	50
Aortic Aneurysm	63	-	3	2	8	2	12	5	6	6	55
Arteriosclerosis and/or Hypertension	114	4	4	3	5	6	9	5	4	-	60
No Cardiovascular Disease	132	7	9	8	3	8	4	1	1	-	59
Total Diagnoses	382										
Total Cases	355	5	5	6	6	6	8	4	3	1	56

Table III

## PRESENTING SYMPTOMS AND COMPLAINTS

Symptom	Percent Distribution by Diagnosis				
	Aortitis (33 Cases)	Aortic Insufficiency (40 Cases)	Aortic Aneurysm (63 Cases)	Arteriosclerosis and/or Hypertension (114 Cases)	No Cardiovascular Disease (132 Cases)
Dyspnea	76	50	54	40	30
Chest pain	39	32	46	20	11
Palpitation	36	42	36	29	17
Cough	21	17	25	2	9
Edema	3	10	10	1	7

Table IV

from aortic aneurysm, aortitis, and arteriosclerosis and hypertension. Eleven per cent of those having no cardiovascular disease were described as having a tambour aortic second sound. The "to and fro" murmur was found most frequently (75) in the cases of aortic insufficiency. In those instances where the "to and fro" murmur was observed in patients with aortitis, a coincidental diagnosis of aortic insufficiency was also made. The aortic systolic murmur has been established as one of the criteria for the diagnosis of luetic aortitis. In this series of observations, the aortic systolic murmur occurred in 30 per cent of patients diagnosed as having luetic aortitis, in 36 per cent diagnosed as having aortic aneurysm, and in 33 per cent diagnosed as having arteriosclerosis or hypertension. It is clear, therefore, that the use of this isolated clinical finding as a means of differentiation between those conditions is not sound. Moreover, 8 per cent of patients who had no demonstrable cardiovascular disease exhibited an aortic systolic murmur as an isolated finding. Signs of arteriosclerosis were evident in a high percentage of all cases except in those having no cardiovascular disease. A dilated aorta was noted fluoroscopically in 60 per cent of the patients diagnosed as having aortitis, in 52 per cent of those with aortic insufficiency, in 62 per cent of those with aneurysm, and in 64 per cent of patients with arteriosclerosis or hypertension. These

data render this isolated sign of doubtful pathognomonic significance for any single diagnostic category. During the period of observation there were differences of opinion as to the presence or absence of a dilated aorta, whether or not the aortic second sound was of tambour quality, and whether or not these changes were due to arteriosclerosis or lues, or in some instances to hypertension.

Fifty-five patients were given yearly cardiovascular examinations while under treatment and in none of these was there demonstrated any regressive changes in the cardiovascular status.

#### COMMENT

In a group of 355 patients observed in a luetic cardiovascular clinic, the age distribution was such that arteriosclerotic changes in the cardiovascular system made the diagnosis of early luetic aortitis practically impossible. The objective criteria for the diagnosis of luetic aortitis may also be fulfilled by hypertensive and arteriosclerotic heart disease without lues, and unless these conditions can be eliminated, the diagnosis of uncomplicated luetic aortitis under average circumstances cannot be made with any degree of assurance. The prevention of the cardiovascular complications of lues is best accomplished by the early adequate treatment of the primary infection.

CHIEF PHYSICAL FINDINGS  
Total Cases 347

Physical Signs	Percent Distribution by Diagnosis				
	Aortitis (33 Cases)	Aortic Insufficiency (40 Cases)	Aortic Aneurysm (63 Cases)	Arteriosclerosis and/or Hypertension (114 Cases)	No Cardiovascular Disease (132 Cases)
Cardiac Enlargement	39	57	43	25	2
Tambour A <sub>2</sub>	39	17	44	33	11
Aortic Murmur: To and fro	33	75	21	2	-
Systolic	30	-	36	33	8
Diastolic	12	25	6	2	1
Signs of Arteriosclerosis	70	68	63	100	19
Dilated Aorta	60	52	62	64	5

Table V

#### REFERENCES

- Berghoff, R. S., Geraci, A. S., and Hirsch, D. A.: Cardiac Syphilis, *Urol. and Cut. Rev.*, 43:46, 1939.
- Bethea, O. W.: Cardiovascular Syphilis, *Urol. and Cut. Rev.*, 43:23, 1939.
- Bruusgaard, E.: Über das Schicksal der Nicht Spezifisch Behandelten Leutiker, *Arch. f. Dermat. u. Syph.*, 157:309, 1929.
- Kemp, J. E., and Cochems, K. D.: Studies in Cardiovascular Syphilis. I. Teleoroentgenography in the Diagnosis of Early Syphilitic Aortitis: A Comparison of Findings in 1,000 Syphilitic and Non-Syphilitic Individuals, *Am. Heart Jour.*, 13:297, 1937.
- Langer, E.: Die Häufigkeit der Leutischen Organveränderungen Insbesondere der Aortitis Leutica, *Münch. en. Med. Wchnschr.*, 73:1782, 1926.
- Levy, R. L., Stroud, W. D., and White, P. D.: Report of Re-examination of 4,994 Men Disqualified for General Military Service, *J.A.M.A.*, 123:937 and 1029, 1943.
- Maynard, E. P., Jr.: The Present Status of the Diagnosis of Uncomplicated Syphilitic Aortitis, *Bull. N. Y. Acad. Med.*, 18:383, 1942.
- Moore, J. E.: The Modern Treatment of Syphilis, C. C. Thomas, 1943.
- Moore, J. E., Danglade, J. H., and Reisinger, J. C.: Treatment of Cardiovascular Syphilis, Results Obtained in 53 Patients with Aortic Aneurysm and in 112 with Aortic Regurgitation, *Arch. Int. Med.*, 49:879-924, 1932.

10. Moore, J. E., and Metildi, P. F.: Uncomplicated Syphilitic Aortitis; Diagnosis, Prognosis and Treatment, *Arch. Int. Med.*, 52:978, 1933.

11. Moore, J. E., Danglede, J. H., and Reisinger, J. C.: Diagnosis of Syphilitic Aortitis Uncomplicated by Aortic Regurgitation or Aneurysm; Comparison of Clinical and Necropsy Observations in 105 Patients, *Arch. Int. Med.*, 49:753, 1932.

12. Padgett, Paul and Moore, J. E.: The Results of Treatment in Cardiovascular Syphilis, *Am. Heart Jour.*, 10:1017, 1935.

13. Padgett, Paul and Moore, J. E.: The Roentgenologic Diagnosis of Syphilitic Aortitis, *Am. J. Syph. Gon. and Ven. Dis.*, 21:3, 199, 1937.

14. Parsonnet, A. E., and Bernstein, Arthur: Syphilitic Aortitis, Its Early Recognition, *Urol. and Cut. Rev.*, 44:499, 1940.

15. Scott, Roy W.: Cardiovascular Syphilis, *Amer. Assoc. for Adv. of Science, Publ.* 6, pp. 118-122, 1938.

16. Thompson, W. P., Comeau, W. J., and White, P. D.: The Role of the Treatment of Syphilis in the Prevention of Cardiovascular Involvement, *Am. Heart Jour.*, 17:286, 1939.

17. Turner, T. B.: The Race and Sex Distribution of the Lesions of Syphilis in 10,000 Cases, *Bull. Johns. Hopkins Hosp.*, 46:159, 1930.

18. Warthin, A. S.: The Lesions of Latent Syphilis, *South. M. J.*, 24:273, 1941.

## Physiology of Traumatic Reflexes and Respiration During Surgical Anesthesia\*

OBSERVATIONS MADE UNDER PENTOTHAL AND LOCAL NERVE BLOCK

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THIS report is based on a succession of clinical observations made during the past two and a half years, in which time the combined use of intravenous pentothal sodium and local nerve block provided the anesthesia of choice for 70 per cent of general surgical cases. Admittedly this present work reflects the viewpoint and perspective of the surgeon. For this reason the indulgence of the professional anesthetist is asked for any gross shortcomings in the accompanying interpretation of physiologic phenomena. The facts, nevertheless, are distinct and stand by themselves.

There is, however, a certain advantage in the surgeon's approach to the problem of the physiology of surgical anesthesia. The surgeon is in a position to continue and project into this clinical field his background of training in experimental physiology; he may at once initiate, observe and record variations in physiologic response to surgical trauma; he may at will functionally denervate with injections of procaine, selected neurogenic areas, thus eliciting contrasting physiologic responses from which he may bring evidence to bear on the problem of specific pathways of nerve impulse conduction. With these potentialities at hand, the surgeon should contribute largely to the basic problem of the physiology of surgical anesthesia.

The introduction of intravenous pentothal sodium anesthesia by Lundy a decade ago contributed not only a new agent of great value, but it provided also a new opportunity for the study of the physiology of surgical anesthesia. This enlarged opportunity is based on the selective pharmacologic action of the drug. Pentothal sodium exerts its major depressing effect on the cerebral cortex and on the thalamus. It thus in effect estab-

lishes a functional decerebration of the surgical patient. The physiologic status of the patient under pentothal sodium anesthesia is quite comparable from the viewpoint of reflex studies, to the surgically decerebrated animal. By virtue of this restricted primary local pharmacologic action at and above the level of the thalamus, all reflex arcs between the vital centers in the bulb (i.e., respiratory center) and the periphery remain intact. The additional graded depressing action of this drug on the respiratory center in the medulla, and its concomitant lack of action on the conduction pathways of the nervous system below the bulb, create a unique opportunity for accurate estimation of the interrelationship existing between peripheral traumatic stimuli of surgical origin and observable respiratory responses.

This situation with pentothal anesthesia stands in sharp contrast with the condition prevailing under ether anesthesia. With ether the conduction pathways distal from the bulb are depressed even to the point of establishing paralysis in the areas of distribution of the intercostal nerves. Also the local irritation of the air passages by ether fumes initiates afferent impulses in the pulmonary vagal reflex arcs which strongly stimulate respiration and distort completely the picture of simple traumatic reflex stimulation of respiration. Spinal anesthesia by its massive point suppression of afferent impulses at the juncture of the peripheral nerves with the spinal cord, eliminates all possibility of central conduction of nerve impulses of peripheral origin, thus abruptly terminating any possibility of studying such reflex actions. Regardless of the opinion which one holds concerning the value of pentothal sodium as a general anesthetic agent, the drug does provide an approach to the study of the physiology of anesthesia during the course of surgical procedures which is not equaled by any other anesthetic agent.

The identification of surgical trauma as the

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